

Opioid Treatment Programs in Indiana – The Use of Medication in Addiction Treatment

Addiction to opioids (e.g., heroin, morphine, prescription pain relievers) is a serious health problem with wide-ranging social and economic implications. In 2010, more than 2 million Americans were affected, with 1.9 million U.S. residents addicted to prescription opioids and 359,000 addicted to heroin. Abuse of opioids, particularly heroin, has been associated with unintentional overdoses and transmission of hepatitis, HIV, and sexually transmitted diseases [1].

Interventions that have been found effective in patients with opioid dependence include opioid treatment programs (OTPs). OTPs are medication-assisted approaches that use pharmaceuticals (primarily methadone and buprenorphine), in combination with counseling and other supportive services to treat severe, chronic, and long-term opioid addiction; this may include detoxification from short-acting opioids, medically supervised withdrawal treatments, and pharmacotherapy to stabilize patients [2]. Since controlled substances are dispensed as part of the program, OTPs are highly regulated by federal as well as state agencies [3].

The use of medications to treat addiction is controversial, because many view addiction not as a disease, but as a choice made by the user, and also because of the belief that this type of treatment represents trading one addiction (e.g., heroin) for another (e.g., methadone) [4]. OTPs are often further stigmatized because they are thought to “bring down” the area around them by attracting “undesirable” people, which will subsequently increase crime and drug dealing rates [4, 5].

Currently, there are 1,200 OTPs in the United States, with the heaviest concentration found in the Eastern regions [6]. In Indiana, there are 13 OTPs under the state’s supervision. The number of patients treated in Indiana’s programs quadrupled from 3,646 in 1998 to 14,269 in 2011 (this excludes the Richard L. Roudebush Medical Center, which is operated by the U.S. Veterans Administration). Historically, patients entering Indiana’s OTPs were predominately males and non-Hispanic whites; most were Indiana residents, but services were also provided to patients from surrounding states [3, 7].

OTPs are highly regulated in the United States and must be registered with the Drug Enforcement Administration (DEA) [8, 9]. Additionally, addiction treatment providers in Indiana have to be certified by the Family and Social Services Administration’s Division of Mental Health and Addiction [9]. Indiana law currently prohibits

the establishment of new OTPs in the state [3, 10].

The focus of this policy brief is on methadone and buprenorphine in the treatment of opioid addiction and not on their use in pain management. Though some physicians still utilize these analgesics to relieve patients’ pain, the drugs are primarily used in OTP settings [11, 12].

What are Opioids?

Opioids are psychoactive substances with analgesic (pain relieving) properties that bind to opioid receptors located primarily in the brain, spinal cord, and digestive tract. Opioids are among the oldest known drugs. Opium and its derivatives have been used for thousands of years in medicine [13].

Although ‘opiate’ and ‘opioid’ are often used interchangeably, there is a clear distinction between the terms. Opiates are natural alkaloids that are derived directly from opium (the opium poppy, *Papaver somniferum*), including morphine (and its further derivative, heroin) and codeine [13, 14]. In contrast, opioids are a much broader category and include (a) opiates; (b) synthetically derived opioids that emulate the effects of natural opium (though chemically different) and can be classified as either semi-synthetic (e.g., oxycodone, buprenorphine) or fully-synthetic (e.g., methadone, fentanyl); and (c) naturally occurring endogenous opioids within the human body, such as endorphins [14].

Adverse effects of opioid use include drowsiness, mental confusion, nausea, constipation, and, depending on the amount of drug taken, respiratory depression [15, 16]. For some users, opioids produce a euphoric effect, since these drugs also affect the reward areas of the brain, hence reinforcing the drug’s addiction potential. Opioids can be effective in managing pain when taken as prescribed, and addiction rarely occurs when used properly for short-term medical purposes [16]. When opioids are consumed in large doses, serious health problems such as severe respiratory depression and death can result. Also, when taken over long periods of time, opioids can potentially lead to physical dependence and addiction [16].

Medication-Assisted Treatment

Methadone, buprenorphine, and (in some cases) naltrexone have been found effective in treating opioid addiction. These pharma-



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ceuticals work by binding to opioid receptors and (a) suppressing withdrawal symptoms and cravings (agonistic action), or (b) blocking the effects of other opioids such as heroin and morphine (antagonistic action). The benefits of medication-assisted treatment are that these pharmaceuticals (1) decrease compulsive drug-seeking behaviors and hence reduce related criminal activities; (2) decrease risky behaviors, such as injection drug use (IDU), needle-sharing, and high-risk sexual activities; and (3) help patients to become more receptive to counseling and behavioral approaches [17-19].

Methadone, a Schedule-II narcotic, is a synthetic opioid analgesic that traditionally has been used for pain relief [20-24], but now is primarily utilized in the treatment of opioid dependence.

Buprenorphine, a Schedule-III narcotic, has been increasingly used as a safe alternative to methadone in treating opioid dependence [24-26], because of buprenorphine’s “ceiling effect;” i.e., after reaching a plateau, any increased dosage of the drug will have little to no effect on the user, resulting in a lower risk of abuse, addiction, and adverse effects, such as lower toxicity from overdose [25-28]. Unlike methadone treatment, which requires the patient to visit a licensed methadone clinic, buprenorphine can be dispensed by physicians in office-based settings once they have completed a specialized, eight-hour training [29].

Dispensation of Methadone and Buprenorphine over the Past Decade

The number of methadone and buprenorphine prescriptions dispensed has increased considerably in the United States. Methadone prescriptions nationwide rose from 863,039 in 2000 to 4,439,850 in 2008, a 400-percent increase. Although methadone is primarily utilized now as a maintenance treatment for opioid addiction, some physicians still prescribe it to treat pain [12]. The use of buprenorphine also increased substantially; from 2004 to 2008, prescriptions for Suboxone® rose from 225,014 to 3,154,795 (a 1,300-percent increase), while prescriptions for Subutex® rose from 42,211 to 263,878 (a 500-percent increase) during that time period [30]. Nearly one-fourth of U.S. residents in substance abuse facilities received methadone or buprenorphine in 2007; of these, the majority (262,684 persons or 99 percent) received methadone [30].

In Indiana, 13,485 patients received pharmacological opioid treatments in 2009. Buprenorphine was used at seven OTPs for 155 patients that year, representing only 1.2 percent of all treated patients at Indiana OTPs; all others were treated with methadone. As a result of treatment, the following percentages of the treatment population showed improvement in the recovery indicator categories below:

- 67.1 percent eliminated or reduced illicit use of prescription opioid drugs;
- 74.4 percent eliminated or reduced use of non-prescription opioid drugs, predominantly heroin;

- 69.1 percent eliminated or reduced illicit use of drugs other than opioids;
- 71.5 percent eliminated or reduced criminal behavior;
- 74.0 percent eliminated or reduced risky behavior related to spread of infectious disease;
- 64.8 percent eliminated or reduced alcohol abuse;
- 45.1 percent improved education or vocational training;
- 56.9 percent improved employment status; and
- 74.3 percent improved family and social relationships [3].

In Indiana, more than 12.7 million prescription drugs (i.e., controlled substances, Schedules-II to V) were dispensed in 2011, including 117,453 prescriptions for methadone (0.9 percent of all controlled substances) and 33,413 prescriptions for buprenorphine (0.3 percent of all controlled substances) (see Table 1) [31]. Compared to buprenorphine, methadone has lower treatment costs; is more effective in treating patients with higher tolerance to opioids; and has generally higher treatment retention rates [28, 32]. Buprenorphine, on the other hand, is safer and has a lower risk of toxicity; opioid withdrawal is less severe after stopping treatment as compared to methadone; the drug has a lower abuse potential; and it is available through primary care physicians in office-based treatment [28, 32].

Table 1: Number of Controlled Substances Dispensed in Indiana (INSPECT, 2008-2011)

	2008	2009	2010	2011
Methadone	110,237	118,038	104,468	117,453
Buprenorphine	2,582	5,549	27,462	33,413
All Controlled Substances	11,635,092	12,713,931	11,341,539	12,743,236

Source: Indiana Board of Pharmacy [31]

Nonmedical Use of Opioids and its Consequences

Opioid abuse can result from both the use of illegal (e.g., heroin) and legal substances (e.g., prescription opioid pain relievers). In Indiana, 1.1 percent of residents ages 12 and older used heroin at least once in their life, 0.2 percent used it in the past year, and less than 0.01 percent used it in the past month [33]. Prevalence rates for nonmedical prescription pain reliever use were considerably higher, with 15.0 percent of residents ages 12 and older reporting lifetime use, 6.1 percent of residents reporting past year use, and 2.0 percent residents reporting past month use [33].¹

Results from the 2009 Treatment Episode Dataset (TEDS) show that nonmedical methadone use did not play a major role in treatment admissions for standard (i.e., non-OTP) services. Nonmedical methadone use was only reported in 0.7 percent of all treatment admissions in Indiana (U.S.: 0.7 percent); and percentages were higher among females (1.0 percent) than males (0.6 percent), and among whites (0.9 percent) than blacks (0.2 percent) or other races

¹ Estimates are based on annual NSDUH averages from 2002 through 2004 and are the most recent state-level data available.

(0.5 percent) [34].

Since methadone is normally prescribed as a treatment for opioid addiction, some patients consider it less dangerous than illicit drugs, such as heroin [22]. This misperception can result in accidental overdoses because the drug has no “ceiling effect,” that is, at high doses, methadone may cause depressed respiration, vomiting, fluid accumulation in the lungs (pulmonary edema), heart attacks (cardiac arrhythmias), or death [22, 28, 30, 32]. Approximately 70 percent of methadone-related deaths in the United States were due to nonmedical or diverted use [22]. Some patients have reported unintended side-effects with methadone treatment, including discomfort, numbing, fatigue, and impaired memory [22]. Buprenorphine is generally considered safer than methadone, because as a partial opioid agonist it has a ceiling effect; that is, the drug’s maximal effects are less than that of a full agonist and will plateau at a maximum level, even with further increases in dosage [22, 25-27]. Patients taking buprenorphine in detoxification treatment programs have reported less severe withdrawal symptoms from cessation of treatment than when they were prescribed methadone [22].

In 2007 in the U.S., there were almost 4 million drug-related emergency department (ED) visits, and 483,612 of these involved narcotic analgesics [30]. The number of ED visits for methadone increased from 48,864 visits in 2004 to 69,506 visits in 2007; 78 percent of methadone-related ED visits in 2007 were due to nonmedical use, while 7 percent involved patients who had adverse reactions to the medication. ED visits for buprenorphine (including its combinations with naloxone) increased from 1,001 in 2004 to 10,229 in 2007; 70 percent were attributable to nonmedical use, while 16 percent were caused by adverse drug reactions [30].

Combining methadone or buprenorphine with additional drugs can be particularly harmful. The use of opioids together with other drugs that depress the central nervous system can result in reduced heart and respiration rates, and may potentially lead to death. Between 2004 and 2007, there was an 83 percent increase in ED visits that involved methadone in combination with other pharmaceutical drugs. During the same time period, there was a 233 percent increase in cases involving combinations of methadone, alcohol, illicit drugs, as well as other pharmaceuticals [30].

Low overdose mortality has been reported with both methadone and buprenorphine. A study from Germany noted that overdose mortality was lower in groups receiving either drug in treatment compared to those taking the drugs outside of a treatment setting [32]. Between 2000 and 2008, 654 deaths due to methadone were reported to U.S. poison control centers, and 9 deaths due to buprenorphine were reported during that same time period [30].

Cost-Effectiveness of Opioid Treatment Programs

Numerous studies have shown the effectiveness of medication-assisted approaches in addiction treatment. Methadone, which has been officially recognized as a potential substitution therapy for illicit narcotic use since the 1960s, has been the most systematically studied and successful pharmacotherapy for treating patients with opioid addiction [23, 35]. Positive outcomes of methadone or buprenorphine treatments include a decrease in clients’ treatment dropout rates; a decrease in the use of opioids and other substances; a decrease in health problems; and a decrease in high-risk behaviors, including needle-sharing among injection drug users and unprotected sexual activity. Also, those in treatment are more likely to be employed fulltime [18, 19, 35-42].

Opioid dependence, and its effects on individuals, families, and society, has been estimated at \$20 billion per year [43]. The cost on the healthcare system alone is estimated at \$1.2 billion per year [43]. An important consideration in health policy decision-making is the cost-effectiveness of treatment.

One study found a 4:1 return on taxpayer dollars for methadone maintenance and inpatient treatment of opioid dependence [43]. Those patients who are enrolled in methadone maintenance programs have been shown to make more than twice the amount of earnings from jobs than those opioid-dependent patients not enrolled in treatment. Reduction in overall crime rates for patients in opioid replacement programs have also resulted in additional cost savings to society [22, 43].

Another study indicated that even a small addition of slots in methadone maintenance programs would be cost-effective, even at twice the cost and half the effectiveness rate of current methadone maintenance programs [44].

OTPs and HIV

Injection drug use (IDU), typically associated with heroin use, has been linked to increased rates of HIV, hepatitis C, tuberculosis, and sexually transmitted diseases (STDs) [43]. In 2008, IDU was associated with 12.9 percent of all new HIV cases, of which about one-fourth were among women and adolescents [6]. Many patients in HIV treatment centers are also dependent on opioids [45, 46].

When patients enter O'TPs, they go through an extensive medical background/history check and physical medical examination to determine such things as length of stay and dosage of opioid treatment drugs in the program [47]. A complete medical record of the patient is produced, which includes a determination if the patient had been exposed to such diseases as HIV [47]. O'TPs are also required by the federal government to provide counseling on both preventing exposure to and transmission of HIV for every patient admitted (or readmitted) to a maintenance or detoxification treatment [6, 8, 47, 48].

Methadone maintenance programs have been cited as decreasing the likelihood a patient will become HIV positive through both sexual- and injection-related means, though less is known about the effects of other treatment programs on HIV reduction [43, 49]. Studies have shown that the integration of HIV treatment and substance programs may improve the overall health of a patient through both a reduction in risk behaviors associated with contracting HIV and a reduction in substance abuse generally [6, 44]. Furthermore, separating HIV treatment from substance abuse treatment has been posited to lead to a miscommunication among the different healthcare providers, possibly resulting in patient-provider conflict; unintended adverse poly-drug interactions; and overall decreased benefits of either treatment program [6].

Buprenorphine has been shown to have less adverse effects overall than methadone and fewer drug-drug reactions among HIV patients concurrently treated with antiretroviral medication [6, 27]. Buprenorphine therapy may be a possibility for opioid-dependent patients at HIV treatment facilities, since the medication can be dispensed in office-based settings by prescription [6, 49]. HIV treatment facilities that are interested in prescribing buprenorphine must obtain a special waiver directly from the Substance Abuse and Mental Health Services Administration (SAMHSA) [6, 50].

Pregnancy and Opioid Replacement Therapy

Opiate use during pregnancy may result in premature deliveries that have serious complications, as well as delayed child development and reduced parenting skills on the part of the mother [43]. Studies have indicated that anywhere from 60 to 90 percent of infants born to mothers who abuse drugs experience withdrawal symptoms, though the biochemical and physiological processes governing withdrawal are still poorly understood [22]. In addition, women who engage in IDU have been reported to give birth to children who represent over half of all pediatric AIDS cases [43]. It is estimated that 75 percent of all new HIV cases for women and children are attributed to IDU [44].

Women in methadone maintenance therapies are more likely to receive prenatal care for their unborn children than those women not currently enrolled in opioid treatment programs [43]. Prenatal care can include antiretroviral therapies that can reduce the transmission of HIV during pregnancy from mother to child [43]. Opioid replacement therapy has also been associated with improved outcomes in pregnant women, including greater gestational age, higher birth weight, and fewer consequences compared to IDU [27].

Normally, prior to admittance to an O'TP, patients must be addicted to opiates for a one-year period per DSM-IV² addiction guidelines [8, 51]. Pregnant women may get an exception to the federal one-year rule and enter treatment much sooner by having a program physician certify their pregnancy [8]. Once enrolled in O'TPs, pregnant women are to be given both gender-specific services and prenatal care, either through the O'TP directly or through referral to other healthcare providers [8]. A preference is also given to pregnant women to be enrolled in interim maintenance treatment, if they are unable to be placed in a public or private O'TP both within a reasonable geographic area and 14 days after submitting an application for entrance into a treatment program [8].

Children born to mothers on methadone treatment are at a high risk for developing neonatal abstinence syndrome (NAS), also known as neonatal withdrawal [27]. Though buprenorphine studies are not as numerous as those on methadone (due to the current use for opioid treatment beginning in 2002), children born to mothers who were undergoing buprenorphine therapy were less likely to develop severe NAS-related issues than children born to mothers on methadone therapy [22, 27, 30].

²The Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV) is the leading classification manual for mental disorders and illnesses (American Psychiatric Association, 1994). A later text revised edition was also released and is referred to as the DSM-IV-TR (American Psychiatric Association, 2000).

Barriers to Treatment and Public Policy Concerns

Nationally, the demand for OTPs often exceeds treatment availability and some programs have waiting lists for services. Longer waiting times for patients can increase stress and reduce the likelihood of patients actually entering treatment [52]. Only an estimated 15 percent of those in need of opioid dependence treatment are able to enter existing programs and people can be on waiting lists for months in some areas [53]. Fortunately, Indiana OTPs have the capacity to treat those in need of their services and do not need to employ waiting lists.

A policy-related criticism of OTPs is that some view methadone maintenance as just substituting one drug for another. However, the scientific evidence clearly suggests that proper methadone maintenance, when compared to other medical treatments, can help to reduce both the medical and social harms produced by opioid abuse [53].

Another criticism is that methadone maintenance programs do not result in a total discontinuation of injection drug use. In fact, only around 3.5 percent of patients per year enrolled in treatment programs completely stop IDU [44]. Nevertheless, these programs have been shown to reduce the spread of HIV [44]. Studies have shown that the reduction of behaviors associated with contracting HIV associated with methadone maintenance programs are more cost-effective than other types of HIV risk behavior reduction programs (e.g., educational or voluntary screening programs) [44].

Though buprenorphine has been shown to be a highly effective treatment for opioid addiction, it is not in widespread use in treatment [25, 26, 54]. One study showed that within four years of buprenorphine entering the market as an opioid treatment, 75 percent of treatment facilities surveyed in four large metropolitan areas chose not to implement buprenorphine [54]. Educating the treatment organizations on newer types of opioid dependence medications may not be enough. Many organizations are hesitant to switch from methadone, which has been used for years as a treatment, to buprenorphine [54]. One significant reason for treatment organizations resisting new treatments is their “cultural system,” which incorporates the attitudes, philosophy, and goals that shape what sort of treatment (including medication) is offered in treatment organizations [54].

Another potential barrier is treatment cost. In the United States, buprenorphine treatment alone (without counseling or ancillary services) is estimated at \$200 per month per patient, compared to \$30 for methadone [28, 29]. In Indiana, the estimated annual out-

of-pocket expenses per patient, including medication, counseling, drug testing, and other supportive services, was \$3,467-\$4,829 for methadone maintenance and \$6,640 for buprenorphine treatment, in 2009 [3].

Thoughts for Policymakers

Opioid dependence is a public health concern that costs society billions of dollars in direct and indirect costs [43]. Research shows that effective treatments, such as OTPs, can reduce drug use, overdose deaths, and crime; increase social productivity; and prevent the spread of infectious diseases, including HIV [53]. Current Indiana law states that no new OTPs can be established in the state, potentially affecting access for people who do not live near treatment locations [3]. To increase the effectiveness of and access to opioid treatment, implementation of evidence-based programs, policies, and procedures are recommended [3-5, 53-55], as follows:

- Establish a comprehensive opioid treatment policy that combines education, the dispelling of misconceptions about opioid addiction treatment, and the required use of new, effective treatments such as buprenorphine.
- Remove the current ban on creating new OTPs in the state, so that these treatment modalities can be promptly established to offer services, should the need arise.
- Integrate substance abuse treatment into healthcare and expand recovery services (e.g., expanding addiction treatment in Community Health Centers) while creating training opportunities to increase access. Under the Affordable Care Act, insurance companies will be required to address drug addiction as both a preventable and treatable ailment.

Opioid dependence is a serious and complex issue that affects thousands of Indiana residents per year [33]. Though OTPs can be effective in treating opioid dependence, their work is often misunderstood. Policies that help dispel the stigma that these treatment facilities and their patients face, while expanding new and effective opioid abuse treatments, will be crucial in treating opioid addiction and reducing its negative consequences.

These policy recommendations only focus on the use of pharmaceuticals, such as methadone and buprenorphine, as a treatment option for opioid dependence and not for pain management. The challenges involved in treating pain, particularly non-cancer chronic pain, are manifold and not addressed in this issue brief.

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The mission of the Center for Health Policy is to conduct research on critical health-related issues and translate data into evidence-based policy recommendations to improve community health. The CHP faculty and staff collaborate with public and private partners to conduct quality data driven program evaluation and applied research analysis on relevant public health issues. The Center serves as a bridge between academic health researchers and federal, state and local government as well as healthcare and community organizations.

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